PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2007/011435	10.05.2007	10.05.2006

International Patent Classification (IPC) or both national classification and IPC
INV. C07H21/00 C12N15/11

Applicant
AVI BIOPHARMA, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	see form PCT/ISA/210	de Nooy, Arjan Telephone No. +31 70 340-2338

Form (PCT/ISA/237) (Cover Sheet) (April 2005)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2007/011435

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5,6,14-16,20, 37-39,41
	No:	Claims	1-4, 7-13, 15-19, 21-36, 40, 42
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-42
Industrial applicability (IA)	Yes:	Claims	1-42
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V.

Reference is made to the following document:

D1 : WO 2006/047683 A (AVI BIOPHARMA INC [US]; STEIN DAVID A [US]; GE QING [US]; CHEN JIANZHU) 4 May 2006 (2006-05-04)

Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 and claims where the link is b1 is not new in the sense of Article 33(2) PCT.

Document D1 (e.g. figure 2H) discloses oligomers comprising a sequence of morpholino subunits where the link between the morpholino subunit has a cationic piperazino group as in claim 1 (b1). Those compounds are used in antisense therapy and may contain a petide transport moiety as in claim 22. Therefore, claims 1-4, 7-13, 15-19, 21-36, 40 and 42 lack novelty in view of Art. 33(2) PCT.

Inventive step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-42 does not involve an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claim 1-42, and discloses antisense oligomers comprising a sequence of morpholino subunits where the link between the morpholino subunit has a cationic piperazino group as in claim 1 (b1). On page 22 of D1, line 30-32, also a N,N-diethylenediamine phosphoramidate linkage is mentioned.

The subject-matter of claims 1-42, inasfar as they are different from D1, differs from this known subject matter in that other positively charged nitrogen amine containing phosphoramidate linkages between the morpholino subunits are applied.

The technical effect of this difference is not known.

The problem to be solved by the present invention may therefore be regarded as the provision of further compounds for antisense therapy.

The solution proposed in claims 1-42 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

in order to solve the above problem, the skilled person would indeed try various amine containing linkages other than the ones disclosed in D1. The fact that D1 mentions also an alternative cationic linkage can be seen as a clear incentive for the skilled person. Therfore, no inventive activity is present in claims 1-42.